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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,821	02/25/2002	Jay D. Hunt III	00M28. 1 Hunt	1308

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PATENT DEPARTMENT
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EXAMINER	
JONES, DWAYNE C	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,821	HUNT ET AL.	
	Examiner	Art Unit	
	Dwayne C. Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-10 are pending.

2. Claims 1-10 are rejected.

Response to Arguments

3. Applicants' arguments filed November 26, 2004 have been fully considered but they are not considered persuasive with respect to the rejections under 35 U.S.C. 112, first paragraph. Applicants argue the following arguments. First, applicants allege that there is adequate written description in the instant specification for the functionally written phrase, "a bFGF-active PAF antagonist." Second, applicants purport that because instant claim 1 is not directed to inhibiting the growth of any tumor but rather to inhibiting the growth of a tumor that depends on basic fibroblast growth factor-stimulated angiogenesis. Third, applicants suggest that the cancer is predictable, which is not found persuasive and convincing. Fourth, applicants submit that the breadth of the claims is not broad. Fifth, applicants argue that there is ample direction and guidance to support these instantly broad claims. Sixth, applicants even allege that the quantity of experimentation is not unreasonable to practice the claimed technology.

4. First, applicants allege that there is adequate written description in the instant specification for the functionally written phrase, "a bFGF-active PAF antagonist." Although there is support for phrase a bFGF-active PAF antagonist for the compounds of BN-50730 and CV 3988, the instant specification has insufficient descriptive support

for the broad functional phrase of a "bFGF-active PAF antagonist" in the instant specification. In addition, the instant specification does not describe what is meant by the functional characteristics of being known as a bFGF-active PAF antagonist. Moreover, the phrase, "a bFGF-active PAF antagonist" not only functionally describes compounds at the time of the filing of this invention but also embraces compounds not yet known or discovered. Applicants also have not provided one skilled in the art with any structural identifying characteristics of the phrase a "bFGF-active PAF antagonist." Because there is no evidence, such as with review articles or assays, that there is any per se structure/function relationship between the disclosed phrase of a "bFGF-active PAF antagonist" and any others that might be found using the claimed method, the instant specification fails to adequately describe this broad functional recitation of compounds other than the compounds of BN-50730 and CV 3988. In addition, there is on adequate written description of functionally described bFGF-active PAF antagonist that are derivatized and/or functionalized with other moieties such as with other organic compounds, carbohydrates, antibodies, amino acids, peptides. Thus, the instantly filed specification fails to provide an adequate written description to provide the skilled artisan with an actual reduction to practice of all embodiments that are embraced by the breadth of any antagonist that is functionally described as being known as a "bFGF-active PAF antagonist."

5. Second, applicants purport that because instant claim 1 is not directed to inhibiting the growth of any tumor but rather to inhibiting the growth of a tumor that depends on basic fibroblast growth factor-stimulated angiogenesis. The only inhibiting

tumors of carcinoma that are enabled in the present specification are those of lung and prostate cancer *and only* with the administration of bFGF-active PAF antagonist compound of BN-50730. In addition, this is supported by the administration of BN-50703 to mice that were implanted with human prostatic carcinoma cells, PC-3, and the lung adenocarcinoma cell line 201T, (see Examples 7 and 3, respectively). Accordingly, there is no correlation between the administration of all, let alone future, bFGF-active PAF antagonist compounds for the treatment of numerous types of cancers. This is supported by the fact that the instant specification only has support and guidance for treatment of only lung and prostate cancer and only with the administration of bFGF-active PAF antagonist compound of BN-50730. For these reasons and those of record, one skilled in the art is not provided

6. Third, applicants suggest that the cancer is predictable, which is not found persuasive and convincing. The cancer art is highly unpredictable, for example as to the methods and modes of treating cancers, the metastasis of cancer, and even the development of drug resistant cancer. In addition, the compounds of the inventions are functionally described as being known as "bFGF-active PAF antagonist."

7. Fourth, applicants submit that the breadth of the claims is not broad, despite the fact that the instant specification only teaches of two working examples for treating lung and prostate cancer *and only* with the administration of bFGF-active PAF antagonist compound of BN-50730. In addition, this is supported by the administration of BN-50703 to mice that were implanted with human prostatic carcinoma cells, PC-3, and the

lung adenocarcinoma cell line 201T, (see Examples 7 and 3, respectively of the instant specification). For these reasons, this argument is not found persuasive.

8. Fifth, applicants argue that there is ample direction and guidance to support these instantly broad claims. The compounds of the inventions are functionally described as being known as substances as being known as "bFGF-active PAF antagonist." Moreover, due to the fact that the specification only provides guidance to treating lung and prostate cancer *and only* with the administration of only one bFGF-active PAF antagonist compound of BN-50730, the skilled artisan is not provide with ample direction and guidance to treat every and all cancers and with the administration of any compound that is embraced by the broad functional recitation of any and all compounds that any antagonize bFGF-active PAF, and with any combination of any and all anti-cancer agents that inhibit angiogenesis.

9. Sixth, applicants even allege that the quantity of experimentation is not unreasonable to practice the claimed technology. However, given the fact that applicants' specification only provides the one skilled in the art with only two examples of cancer that is compounded with a showing of the administration of only with the administration of only one bFGF-active PAF antagonist compound of BN-50730, the skilled artisan is forced to conduct numerous and undue experiments to not only determine what types of cancers are effectively treated but also what specific compounds other BN-5030, can be administered for treating all cancers, (see pages 19 and 25-26, respectively in the instant specification). , (see Examples 7 and 3, respectively of the instant specification).

Claim Rejections - 35 USC § 112

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. The rejection of claims 1, 4, and 6-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and repeated for both the above-stated and reasons of record. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claim 1 is directed to a method of inhibiting the growth of a tumor in a mammal, wherein the growth of the tumor depends on basic fibroblast growth factor-stimulated angiogenesis with the administration of a bFGF-active PAF antagonist. This claim fails to meet the written description requirement for the following reasons. The term a bFGF-active PAF antagonist is written functionally. There is insufficient descriptive support for the functional term a bFGF-active PAF antagonist in the instant specification. In addition, the instant specification does not describe what is meant by the functional characteristics of being known as a bFGF-active PAF antagonist. Structural identifying characteristics of the term a bFGF-active PAF antagonist are not disclosed to one skilled in the art. There is no evidence that there is any per se structure/function relationship between the disclosed term of a bFGF-active PAF antagonist and any others that might be found using the claimed method. Furthermore, there is no support that the particularly disclosed term of a bFGF-active PAF antagonist is represented by

the sole examples of BN-50730 and CV 3988. Thus, these claims fail to comply with the written description requirement. In the absence of some understanding of the functional term a bFGF-active PAF antagonist other than the adequately described BN-50730 and CV 3988, the artisan would not have accepted that the applicant was in possession of the claimed method as currently written.

12. The rejection of claims 1-8 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting tumors of carcinoma of the lung and prostate and only for , does not reasonably provide enablement for carcinomas of the breast, colon, stomach, pancreas, skin, uterus, cervix, mouth, larnyx, esophagus, liver, kidney; sarcomas of the muscle or connective tissue; osteosarcomas; neuroblastomas; glioblastomas; neuroblastomas; Hodgkin's disease lymphomas; non-Hodgkin's lymphomas; B-cell lymphomas; T-cell lymphomas; acute lymphocytic leukemias; chronic myloid leukemia; acute myloid leukemia; and non-malignant tumors is maintained and repeated for both the above-stated and reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the

predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to for inhibiting tumors. The method comprises administering the bFGF-active PAF antagonist compounds of BN-50730.

(2) The state of the prior art

The compounds of the prior art of Montrucchio et al. are directed to inhibiting neovascularization with the PAF receptor antagonist of WEB 2170.

(3) The relative skill of those in the art

The relative skill of those in the art of cancer pharmaceuticals and oncology is very high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often

react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art); In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of treating all tumors prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claim 1 is directed to inhibiting the growth of any tumor with bFGF-active PAF antagonist. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to

DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of a bFGF-active PAF antagonist to be effective in treating or inhibiting the growth of tumors is insufficient for enablement. The specification provides no guidance, in the way of enablement for inhibiting tumors of carcinoma of the lung and prostate, does not reasonably provide enablement for

carcinomas of the breast, colon, stomach, pancreas, skin, uterus, cervix, mouth, larnyx, esophagus, liver, kidney; sarcomas of the muscle or connective tissue; osteosarcomas; neuroblastomas; glioblastomas; neuroblastomas; Hodgkin's disease lymphomas; non-Hodgkin's lymphomas; B-cell lymphomas; T-cell lymphomas; acute lymphocytic leukemias; chronic myloid leukemia; acute myloid leukemia; and non-malignant tumors other than inhibiting tumors of carcinoma of the lung and prostate. The specification provides no guidance, in the way enablement for the treatment or inhibition of tumors of carcinoma of the lung and prostate, does not reasonably provide enablement for carcinomas of the breast, colon, stomach, pancreas, skin, uterus, cervix, mouth, larnyx, esophagus, liver, kidney; sarcomas of the muscle or connective tissue; osteosarcomas; neuroblastomas; glioblastomas; neuroblastomas; Hodgkin's disease lymphomas; non-Hodgkin's lymphomas; B-cell lymphomas; T-cell lymphomas; acute lymphocytic leukemias; chronic myloid leukemia; acute myloid leukemia; and non-malignant tumors. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Accordingly, this is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals

or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses inhibiting tumors of carcinoma of the lung and prostate with the bFGF-active PAF antagonist compounds. However, the instant specification only has enablement for inhibiting tumors of carcinoma of the lung and prostate.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218

(CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the types of tumors that are inhibited with the bFGF-active PAF antagonist compounds that would be enabled in this specification.

13. The rejection of claims 1 and 4-10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn.

Claim Rejections - 35 USC § 102

14. The rejection of claims 1-4 and 8-10 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Hunt et al., abstract 4099, of Proceedings of the American Association of Cancer Research: Cell and Tumor Biology, vol. 41, (2000) is withdrawn in response to the affidavit of November 26, 2004.

Claim Rejections - 35 USC § 103

15. The rejection of claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunt et al., abstract 4099, of Proceedings of the American Association of Cancer Research: Cell and Tumor Biology, vol. 41, (2000) is withdrawn in response to the affidavit of November 26, 2004.

Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Wednesdays, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (571)-273-8300.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application

publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

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DWAYNE JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
March 21, 2005